PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: M. Seul	)	
Serial No. 10/645,426	)	Group Art Unit: 1641
Confirmation No. 8876	)	Examiner: Do, Pensee T.
Filed: 6/21/2003	)	
For: Arrays Formed of Encoded Beads Having Ligands Attached	)	

Commissioner for Patents
PO Box 1450
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Substitute Reply

Dear Sir:

Please review the Examiner's Answer in this matter in light of the comments below. Please ignore the Reply filed on 1/24/2007, and consider this one instead.

A. The Subject Matter of Claims 76-84 and 86-90 Is Nonobvious over Margel in View of Singer et al.

It is noted that the Examiner agrees that the particles in Margel are ***not*** "encoded." The Examiner goes on to state that although the independent claim 76 requires that "different ligands are attached to different particles and said particles are encoded with a chemical or physical characteristic that permits identification of the ligand or ligands attached thereto and permits distinguishing of particles having different ligands attached thereto from each other..."; "Margel teaches that the particles are coated with different ligands in col. 2 line 35 to col. 3, line 5," and goes on to rely on the following passage from the Summary of the Invention:

> [A] solid substrate having covalent bonds to … a multiplicity of layers of at least one species of microspheres, wherein adjoining layers of the multiplicity of layers are covalently linked together, the innermost layer of the multiplicity of layers having the above-mentioned covalent bonds to the solid substrate connected thereto, while at least the outermost layer of the multiplicity of layers contains residual reactive functions. The covalent bonds referred to above may be provided by a ligand denoted "(A)", and the adjoining layers of the multiplicity of layers may be covalently linked together by a connecting ligand denoted "(B)", the ligands (A) and (B) being the same as or different from each other.

This passage only relates to the part of the independent claim 76 reciting "different ligands are attached to different particles …" There is nothing in this passage relevant to the recitation in claim 76 of "said particles are encoded with a chemical or physical characteristic that permits identification of the ligand or ligands attached thereto and permits distinguishing of particles having different ligands attached thereto from each other…" In fact, even if the Margel particles were encoded, one could not ***decode*** such particles (*i.e.*, "[distinguish] … particles having different ligands attached thereto from each other…" as in claim 76) in such a "multiplicity of layers … covalently linked together…" because the upper layers would hide the lower layers from view, and prevent one from ascertaining whether or how the underlying layers of particles were encoded. For this reason, as Applicant noted in the Brief on Appeal, the only remotely relevant portion of Margel is Example 31, where an assay is being conducted with a single layer of protein-coated particles layered on a substrate surface.

The Examiner also agrees that in Example 31 the particles are not in "a planar defined area on the surface of a substrate …" as required in claim 76, but alleges that Margel teaches that the substrate to be coated with particles can be a glass disc (examples 1, 20) or a polypropylene film (example 6). Again, Examples 1, 6 and 20 have nothing to do with assays or encoded particles or the other elements of claim 76. These examples are immaterial and not relevant prior art, because Margel is for the most part directed to microspheres attached to a substrate (as in the title), which may be used for "***immobilizing*** drugs, prodrugs, proteins, biological cells and other controllably releasable substances." *See* Abstract. Encoded particles, decoding particles, and the other elements of claim 76 are not mentioned in the cited examples, or in any other portions of Margel.

The Examiner states that Margel "does not have to teach recording assay signals from individual microparticles" because "the claims … are drawn to a composition, not a method of detecting." The Examiner seems unable to focus on the recitation that "said particles are encoded with a chemical or physical characteristic that permits identification of the ligand or ligands attached thereto and ***permits distinguishing of particles having different ligands attached thereto from each other*** …" One would need to record assay signals from individual microparticles to distinguish them from each other, which the Examiner seems to tacitly agree is not disclosed in Margel.

In response to Applicant's argument that in Singer, neither target or probe is individually encoded, but that only "smears" of fluorescent signals from the cumulative emission of multiple microparticle-labeled probes can be distinguished, the Examiner refers to a portion of Singer describing labeling of bound target, with either red or green-fluorescence emitting microparticle-labeled probes (so as to identify the bound target). The Examiner also states (the following is not a quote from the Singer patent): "If the target is distinguished, then the target complement (ligand) that is bound to such target can also be identified. Therefore, Singer teaches that encoded microparticles can be distinguished individually …" The Examiner's conclusions do not follow from the quoted portion of Singer. As Applicant has noted, the smears of fluorescence resulting from a cumulative signal of microparticles in Singer actually ***prevents*** one from "distinguishing of particles having different ligands attached thereto from each other …" One would only be able to see a cumulative signal; not particles having different ligands, in such case, and this would be especially true in the case set forth in the claims where there are "several different particle-attached ligands" as opposed to just two different types (red or green), in the portion of Singer the Examiner focuses. Accordingly, the Examiner has not refuted Applicant's conclusion that Singer's microparticles cannnot be distinguished individually.

B. The Subject Matter of Claim 85 Is Nonobvious over Margel in View of Singer et al. and Further in View of Nacamulli et al. (US 5,527,710)

In response to Applicant's arguments that Nacamulli et al. do not disclose or suggest encoded, distinguishable particles, and therefore should not be combined with

Margel or Singer (which also do not suggest such particles), the Examiner states "Margel suggested that the substrate can be a semiconducting substrate..." However, the semiconducting substrate in Margel (col. 3, lines 48-49) is not discussed in Example 31 (which relates to assays), but rather relates to the main direction of Margel's invention: for use in immobilization. Nacamulli et al., in contrast, relates to assays monitoring the reaction of antibody-antigen reaction. Accordingly, there is no motivation to combine Nacamulli et al. with Margel.

The remaining rejections, not addressed specifically herein (under Section 112, para. 2, and under Section 103 over the primary references in view of Gombinski) should be reversed for the reasons set forth in the Brief. In conclusion, reversal of all rejections is respectfully requested.

Respectfully Submitted,

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